

**Clean Copy of Amended Specification Page 1**  
**Pursuant to 37 C.F.R. § 1.121(b)(1)(ii)**

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## METHODS FOR DECREASING BETA AMYLOID PROTEIN

### Cross-Reference to Related Applications

This application is a divisional of pending prior application U.S. Serial  
No. 09/239,387 filed January 28, 1999, which is a divisional of U.S. Serial  
5 No. 09/046,235 filed March 23, 1998, now U.S. Patent No. 6,080,778. The  
United States government has certain rights in this invention by virtue of  
National Institutes of Health grant number RO1NS33325 to Bruce A. Yankner.

### **Background of the Invention**

[The United States government has certain rights in this invention by  
10 virtue of National Institutes of Health grant number RO1NS33325 to Bruce A.  
Yankner.]

Alzheimer's disease (AD) is the most common cause of dementia in the  
aged population. The accumulation of large numbers of senile plaques  
containing the 40-42 amino acid amyloid  $\beta$  protein ( $A\beta$ ) is a classic pathological  
15 feature of AD. Both genetic and cell biological findings suggest that the  
accumulation of  $A\beta$  in the brain is the likely cause of AD (Yankner, B.A. (1996)  
Neuron 16, 921-932.; Selkoe, D.J. Science 275, 630-631 (1997)). Strong  
genetic evidence in support of the pathogenic role of  $A\beta$  came from the  
observation that individuals who inherit mutations in the amyloid precursor  
20 protein almost invariably develop AD at an early age. These mutations increase  
the production of a long variant of the  $A\beta$  peptide that forms senile plaques in  
the brain (Goate et al., (1991) Nature 349, 704-706). Mutations and allelic  
variations in other genes that cause AD, including the presenilins and  
apolipoprotein E, also result in increased production or deposition of the  $A\beta$   
25 peptide. Reiman, et al. (1996) N.E.J.Med. 334, 752-758, reported that in middle  
age, early to mid 50's, individuals who are homozygous for the Apo E4 gene  
have reduced glucose metabolism in the same regions of the brain as in patients  
with Alzheimer's disease. These findings suggest that the pathological changes